

CLAIMS

1. A method for stimulating proliferation by a T cell which expresses a cytokine receptor γ chain and which has received a primary activation signal under conditions which normally result in unresponsiveness in a T cell, comprising contacting the T cell with an agent which binds to the cytokine receptor γ chain and stimulates an intracellular signal in the T cell resulting in T cell proliferation, with the proviso that the agent does not consist of natural interleukin-2.

10 2. The method of claim 1, wherein the agent is interleukin-4 or interleukin-7.

3. The method of claim 1, wherein the agent is an anti- γ chain antibody.

4. The method of claim 1, wherein the T cell is contacted *in vivo* with the agent.

15 5. The method of claim 1, further comprising contacting the T cell with both an agent which stimulates a primary activation signal in the T cell and an agent which binds to the γ chain and stimulates an intracellular signal in the T cell.

20 6. The method of claim 5, further comprising contacting the T cell with an agent which stimulates a costimulatory signal in the T cell.

7. The method of claim 5, wherein the agent which stimulates a primary activation signal in the T cell is an antigen.

25 8. The method of claim 7, wherein the antigen is a pathogen selected from the group consisting of a virus, a bacteria, and a parasite.

9. The method of claim 7, wherein the antigen is a tumor antigen.

30 10. The method of claim 7, wherein the T cell is contacted with the antigen *in vivo*.

11. A method for stimulating proliferation by a T cell which expresses a cytokine receptor γ chain and which has received a primary activation signal under conditions which normally result in unresponsiveness in a T cell, comprising contacting the T cell with an agent which acts intracellularly to stimulate phosphorylation of a JAK kinase having a molecular weight of about 116 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis, resulting in proliferation of the T cell.

12. The method of claim 11, wherein the T cell is contacted *in vivo* with the agent.
13. The method of claim 11, further comprising contacting the T cell with both an agent which stimulates a primary activation signal in the T cell and an agent which acts intracellularly to stimulate phosphorylation of a JAK kinase having a molecular weight of about 116 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.
14. The method of claim 13, further comprising contacting the T cell with an agent which stimulates a costimulatory signal in the T cell.
15. The method of claim 14, wherein the agent which stimulates a primary activation signal in the T cell is an antigen.
16. The method of claim 15, wherein the antigen is a pathogen selected from the group consisting of a virus, a bacteria, and a parasite.
17. The method of claim 15, wherein the antigen is a tumor antigen.
18. The method of claim 15, wherein the T cell is contacted with the antigen *in vivo*.
19. A method for inducing unresponsiveness to an antigen in a T cell which expresses a cytokine receptor γ chain comprising contacting the T cell in the presence of an antigen with an agent which inhibits delivery of a signal through the cytokine receptor γ chain resulting in T cell unresponsiveness to the antigen.
20. The method of claim 19, wherein the agent acts extracellularly to inhibit delivery of a signal through the cytokine receptor γ chain.
21. The method of claim 20, wherein the agent binds to the cytokine receptor γ chain without stimulating an intracellular signal in the T cell through the cytokine receptor γ chain.
22. The method of claim 21, wherein the agent is an anti- γ chain antibody.
23. The method of claim 20, wherein the agent binds a natural ligand of the cytokine receptor γ chain to inhibit binding of the ligand to the cytokine receptor γ chain.
24. The method of claim 23, wherein the agent is selected from the group

consisting of an anti-interleukin-2 antibody, an anti-interleukin-4 antibody and an anti-interleukin-7 antibody.

25. The method of claim 19, wherein the agent acts intracellularly to inhibit
5 delivery of a signal through the cytokine receptor γ chain.

26. The method of claim 25, wherein the agent inhibits association of the cytokine receptor γ chain with a JAK kinase having a molecular weight of about 116 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

10 27. The method of claim 25, wherein the agent inhibits tyrosine phosphorylation of a JAK kinase having a molecular weight of about 116 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

15 28. The method of claim 25, wherein the agent inhibits tyrosine phosphorylation of the cytokine receptor γ chain.

20 29. The method of claim 25, wherein the agent inhibits tyrosine phosphorylation of both the cytokine receptor γ chain and a JAK kinase having a molecular weight of about 116 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

30. The method of claim 19, wherein the T cell is contacted *in vivo* with the agent.

25 31. The method of claim 19, further comprising contacting the T cell with the antigen.

32. The method of claim 31, wherein the antigen is an alloantigen.

33. The method of claim 31, wherein the antigen is an autoantigen.

30 34. The method of claim 31, wherein the T cell is contacted with the antigen and the agent *in vitro* and the method further comprises administering the T cell to a subject.

35. The method of claim 34, wherein the antigen is on a surface of an allogeneic or xenogeneic cell and the subject is a recipient of an allogenic or xenogeneic cell.

36. The method of claim 34, wherein the subject is suffering from an autoimmune disease or disorder associated with an inappropriate or abnormal immune response.

37. A method of inhibiting graft-versus-host disease in a bone marrow transplant recipient, comprising contacting a donor T cell which expresses a cytokine receptor γ chain with a cell which expresses a recipient antigen and an agent which inhibits delivery of a signal through the cytokine receptor γ chain on the T cell, resulting in donor T cell unresponsiveness to the cell which expresses the recipient antigen.
- 5
38. The method of claim 37, wherein the agent is an anti- γ chain antibody.
39. The method of claim 37, wherein the agent binds a natural ligand of the cytokine receptor γ chain to inhibit binding of the ligand to the cytokine receptor γ chain.
- 10
40. The method of claim 39, wherein the agent is selected from the group consisting of an anti-interleukin-2 antibody, an anti-interleukin-4 antibody and an anti-interleukin-7 antibody.
- 15
41. The method of claim 39, wherein the agent inhibits association of the cytokine receptor γ chain with a JAK kinase having a molecular weight of about 116 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.
- 20
42. The method of claim 39, wherein the agent inhibits tyrosine phosphorylation of a JAK kinase having a molecular weight of about 116 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.
- 25
43. The method of claim 39, wherein the agent inhibits tyrosine phosphorylation of the cytokine receptor γ chain.
- 30
44. The method of claim 39, wherein the agent inhibits tyrosine phosphorylation of both the cytokine receptor γ chain and a JAK kinase having a molecular weight of about 116 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.
- 35
45. A method for identifying an agent which inhibits delivery of a signal through a cytokine receptor γ chain on a T cell, comprising
- contacting a T cell which expresses a cytokine receptor γ chain with
 - a first agent which stimulates a primary activation signal in the T cell,
 - a second agent which stimulates an intracellular signal through the cytokine receptor γ chain, and
 - a third agent to be tested for the ability to inhibit delivery of the signal through the cytokine receptor γ chain; and

b) determining the presence of T cell proliferation
wherein inhibition of T cell proliferation indicates that the third agent inhibits delivery of a signal to T cell through the cytokine receptor γ chain.

5

46. The method of claim 45, wherein the second agent is a cytokine.

47. The method of claim 46, wherein the cytokine is selected from the group consisting of interleukin-2, interleukin-4 and interleukin-7.

add at *add B37*